WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6: G01N 15/10, 33/50, 15/14, C12O 1/68

(11) International Publication Number:

WO 97/14028

(43) International Publication Date:

17 April 1997 (17.04.97)

(21) International Application Number:

PCT/US96/16198

A3

(22) International Filing Date:

10 October 1996 (10.10.96)

(30) Priority Data:

08/540.814 08/542,401

11 October 1995 (11.10.95) US

11 October 1995 (11.10.95) US

(71) Applicant (for all designated States except US): LUMINEX CORPORATION [US/US]; 12212 Technology Boulevard #K, Austin, TX 78727-6115 (US).

(72) Inventors; and

- (75) Inventors/Applicants (for US only): CHANDLER, Van. S. [US/US]; 2808 McKinney Avenue #410, Dallas, TX 75204 (US). FULTON, R., Jerrold [US/US]; 305 Evergreen Trail, Cedar Hill, TX 75104 (US). CHANDLER, Mark, B. [US/US]; 4 Niles Road, Austin, TX 78700 (US).
- (74) Agent: PATTERSON, Melinda, L.; P.O. Box 4433, Houston, TX 77210 (US).

(81) Designated States: AL, AM, AT, AU, BA, BB, BG, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD. MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published

With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(88) Date of publication of the international search report: 25 September 1997 (25.09.97)

(54) Title: MULTIPLEXED ANALYSIS OF CLINICAL SPECIMENS APPARATUS AND METHOD

(57) Abstract

A method for the multiplexed diagnostic and genetic analysis of enzymes, DNA fragments, antibodies, and other biomolecules comprises the steps of constructing an appropriately labeled beadset, exposing the beadset to a clinical sample, and analyzing the combined sample/beadset by flow cytometry is disclosed. Flow cytometric measurements are used to classify, in real-time, beads within an exposed beadset and textual explanations, based on the accumulated data obtained during real-time analysis, are generated for the user. The inventive technology enables the simultaneous, and automated, detection and interpretation of multiple biomolecules or DNA sequences in real-time while also reducing the cost of performing diagnostic and genetic assays.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AM	Armenia	GB	United Kingdom	MW	Malawi
AT	Austria	GE	Georgia	MX	Mexico
ΑU	Australia	GN	Guinea	NE	Niger
BB	Barbados	GR	Greece	NL	Netherlands
BE	Belgium	HU	Hungary	NO	Norway
BF	Burkina Faso	Œ	Ireland	NZ	New Zealand
BG	Bulgaria	IT	Italy	PL	Poland
BJ	Benin	JP	Japan	PT	Portugal
BR	Brazil	KE	Kenya	RO	Romania
BY	Belarus	KG	Kyrgystan	RU	Russian Federation
CA	Canada	KP	Democratic People's Republic	SD	Sudan
CF	Central African Republic		of Korea	SE	Sweden
CG	Congo	KR	Republic of Korea	SG	Singapore
CH	Switzerland	KZ	Kazakhstan	SI	Slovenia
CI	Côte d'Ivoire	LI	Liechtenstein	SK	Slovakia
CM	Cameroon	LK	Sri Lanka	SN	Senegal
CN	China	LR	Liberia	SZ	Swaziland
CS	Czechoslovakia	LT	Lithuania	TD	Chad
CZ	Czech Republic	LU	Luxembourg	TG	Togo
DE	Germany	LV	Latvia	TJ	Tajikistan
DK	Denmark	MC	Monaco	TT	Trinidad and Tobago
£E	Estonia	MD	Republic of Moldova	UA	Ukraine
ES	Spain	MG	Madagascar	UG	Uganda
FI	Finland	ML	Mali	US	United States of America
FR	France	MN	Mongolia	UZ	Uzbekistan
GA	Gabon	MR	Mauritania	VN	Viet Nam

Internatic Application No PCT/US 96/16198

A. CLASSIFICATION OF SUBJECT MATTER IPC 6 G01N15/10 G01N33 C12Q1/68 G01N33/50 G01N15/14 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) G01N C120 IPC 6 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) C. DOCUMENTS CONSIDERED TO BE RELEVANT Category Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. Х WO 93 02360 A (TRANSMED BIOTECH 1-49.53 INCORPORATED) 4 February 1993 Α see page 4, line 18-31 50 see page 5, line 6-10 see page 6, line 10-25 see page 6, line 26 - page 7, line 8 see page 7, line 18 - page 8, line 2 see page 9, line 31-32 see page 19, line 36 - page 20, line 2 Α WO 89 11101 A (MICHAEL JOHN HOLMES) 16 50-52 November 1989 see page 5, line 20 - page 6, line 15 see page 7, line 33 - page 8, line 2 see page 8, line 15-20 -/--X Further documents are listed in the continuation of box C. X Patent family members are listed in annex. Special categories of cited documents: "I" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the "A" document defining the general state of the art which is not considered to be of particular relevance invention 'E' earlier document but published on or after the international 'X' document of particular relevance; the claimed invention filing date cannot be considered novel or cannot be considered to "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the 'O' document referring to an oral disclosure, use, exhibition or document is combined with one or more other such docu ments, such combination being obvious to a person skilled document published prior to the international filing date but later than the priority date claimed '&' document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report - 6. 08. 97 28 July 1997 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentiaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Zinngrebe, U Fax (+31-70) 340-3016

internatio. Application No PCT/US 96/16198

C.(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	PCT/US 96/16198	
Category *	Citation of document, with indication, where appropriate, of the relevant passages	1	
		Relevant to claim No.	
A	US 4 499 052 A (FULWYLER) 12 February 1985	1-5,30, 35,38, 40,42, 46,50-53	
	see column 1, line 61 - column 2, line 24 see column 6, line 4-11; examples 1,4		
A	US 5 028 545 A (SOINI) 2 July 1991	1-5,30, 35,38, 40,42, 46,50-53	
·	see column 1, line 63 - column 2, line 4 see column 2, line 20-37 see column 2, line 62-66 see column 3, line 10-13 see column 3, line 44-49	40,50-55	
A	US 5 380 663 A (SCHWARTZ ET AL) 10 January 1995	1-5,30, 35,38, 40,42,	
	see column 1, line 30-56 see column 2, line 18-42 see column 2, line 65 - column 3, line 8 see column 4, line 21-28 see column 5, line 8-30 see column 7, line 30 - column 9	46,50-53	
A	US 5 290 707 A (S. WOOD) 1 March 1994 see figure 4	3-5	
A	METHODS IN CELL BIOLOGY, vol. 33, 1 January 1990, pages 613-619, XP000568939 FULWYLER M J ET AL: "FLOW MICROSPHERE IMMUNOASSAY FOR THE QUANTITATIVE AND SIMULTANEOUS DETECTION OF MULTIPLE SOLUBLE ANALYTES" see figure 1E	3-5	
A	EP 0 633 462 A (ORTHO DIAGNOSTIC SYSTEMS) 11 January 1995 see page 2, column 42-49 see page 3, line 39-52 see page 5, line 7-9 see page 5, column 57 - page 6, column 15 see page 9, line 4-10	59	
X	US 4 075 462 A (ROWE WILLIAM GUY) 21 February 1978 see column 10, line 11-42; figure 5	63,64,69	
	-/		
		į.	

Internatio Application No
PCT/US 96/16198

		PCT/US 96/16198
	DOCUMENTS CONSIDERED TO BE RELEVANT	
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 987 539 A (MOORE WAYNE A ET AL) 22 January 1991 see column 1, line 1-20 see column 3, line 51 - column 4, line 32	. 71
A	WO 92 17853 A (PATTERN RECOGNITION L P) 15 October 1992 see abstract see page 3, line 3-19 see page 5, line 3-19 see page 8, line 13 - page 10	71
A	US 5 281 517 A (BACUS ET AL.) 25 January 1994 see column 7, line 1-12 see column 8, line 37-52 see column 13, line 27 - column 14, line 3 see column 21, line 62 - column 22, line 15	72
A	WO 87 06621 A (D. GILLSPIE) 5 November 1987 see page 1, paragraph 2 see page 10, last paragraph - page 11, paragraph 2 see page 12, paragraph 2-5 see page 70, last paragraph - page 73, paragraph 3; figure 6 see page 89, last paragraph - page 90, paragraph 1	75-77,82
A	EP 0 382 433 A (ICI PLC) 16 August 1990 see page 3, line 3-16 see page 4, line 15-33 see page 5, line 32-57	75-77,82
A	EP 0 200 113 A (PANDEX LAB INC) 5 November 1986 see page 11, line 19 - page 14, line 26	75-77,82
A .	US 5 104 791 A (ABBOTT SCOT D ET AL) 14 April 1992 see column 1, line 5-10 see column 4, line 20 - column 5, line 18 see column 5, line 34-50 see column 8, line 26-47 see column 9, line 40-46 see column 10, line 3-27 see column 14, line 20-24	75-77,82

Form PCT/ISA/210 (contunuation of second sheet) (July 1992)

Interr nal application No.

PCT/US 96/16198

Box I	Observations where certain claims were found unsearchable (Continuation of item 1 of item 1 of item 2 of item 2
This Inte	rnational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1.	Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
2.	Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3.	Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II	Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This Int	ernational Searching Authority found multiple inventions in this international application, as follows:
1. 3.	CLAIMS: 1-58,85,89 2. CLAIMS: 59-70,71,74 4. CLAIMS: 75-84
FO	R FURTHER INFORMATION PLEASE SEE FORM PCT/ISA/206 MAILED 01.04.97
1. X	As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.	As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.	No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remar	The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.

information on patent family members

Internatio Application No PCT/US 96/16198

					30/10130
Patent document cited in search repo		ublication date	Patent family member(s)		Publication date
WO 9302360	A . 04-	-02-93 AU CA EP JP US	2348092 2113350 0594763 6509417 5567627	A A T	23-02-93 04-02-93 04-05-94 20-10-94 22-10-96
WO 8911101	A 16-		127231 3565889 1335238 68924064 68924064 0413741 3504276 5585241	A A D T A	15-09-95 29-11-89 18-04-95 05-10-95 08-02-96 27-02-91 19-09-91 17-12-96
US 4499052	A 12-	-02-85 DE FR GB JP JP JP US	3331017 2532431 2126341 1772176 4047265 59060261 4717655	A A,B C B A	08-03-84 02-03-84 21-03-84 14-07-93 03-08-92 06-04-84 05-01-88
US 5028545	A 02-	-07-91 SE DE EP JP SE	458968 3870324 0296136 1035268 8702511	A A A	22-05-89 27-05-92 21-12-88 06-02-89 17-12-88
US 5380663	A 10-	US U	5089416 5084394 5093234 4857451 4774189 4767206 5314824 9100509 5073497 5073498 4918004	A A A A A A A	18-02-92 28-01-92 03-03-92 15-08-89 27-09-88 30-08-88 24-05-94 10-01-91 17-12-91 17-12-91 17-12-91 17-04-90

Information on patent family members

Internatio. Application No
PCT/US 96/16198

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5380663 A		GB 2172104 A,B US 4714682 A US 4868126 A JP 6084969 B JP 61228349 A	10-09-86 22-12-87 19-09-89 26-10-94 11-10-86
US 5290707 A	01-03-94	NONE	
EP 633462 A	11-01-95	CA 2125228 A CA 2141664 A EP 0654160 A WO 9429800 A	09-12-94 22-12-94 24-05-95 22-12-94
US 4075462 A	21-02-78	CA 1050660 A DE 2558392 A FR 2297413 A GB 1497698 A JP 51095884 A	13-03-79 15-07-76 06-08-76 12-01-78 23-08-76
US 4987539 A	22-01-91	AU 2527188 A WO 8900894 A	01-03-89 09-02-89
WO 9217853 A	15-10-92	AU 1791192 A	02-11-92
US 5281517 A	25-01-94	US 5016283 A US 4741043 A US 5018209 A US 5541064 A CA 1312276 A DE 3854644 D DE 3854644 T EP 0317139 A JP 1165958 A US 5086476 A US 4998284 A US 5134662 A DE 3688330 A DE 3689856 D DE 3689856 T EP 0245466 A	14-05-91 26-04-88 21-05-91 30-07-96 05-01-93 07-12-95 13-06-96 24-05-89 29-06-89 04-02-92 05-03-91 28-07-92 27-05-93 30-06-94 08-09-94 19-11-87

information on patent family members

Internatio application No
PCT/US 96/16198

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5281517 A	·	EP 0248840 A	16-12-87
		EP 0571053 A	24-11-93
		JP 2527536 B	28-08-96
		JP 7168102 A	04-07-95
		JP 7146289 A	06-06-95
		JP 7181179 A	21-07-95
		JP 7111425 B	29-11-95
		JP 63501597 T	16-06-88
		US 48878 9 2 A	19-12-89
		WO 8702802 A	07-05-87
		WO 8702803 A	07-05-87
		US 5109429 A	28-04-92
	·	US 5008185 A	16-04-91
		US 5485527 A	16-01-96
		US 5272759 A	21-12-93
		CA 1326601 A	01-02-94
WO 8706621 A	05-11-87	AT 114334 T	15-12-94
		AU 613870 B	15-08-91
		AU 7432987 A	24-11-87
		CA 1301606 A	26-05-92
		DE 3750774 D	05-01-95
		DE 3750774 T	27-04-95
		EP 0305399 A	08-03-89
		JP 2552691 B	13-11-96
		JP 1502317 T	17-08-89
		US 5482834 A	09-01-96
EP 0382433 A	16-08-90	AU 4902590 A	16-08-90
		CA 2009454 A	07-08-90
		GB 2228998 A,B	12-09-90
		JP 2295496 A	06-12-90
EP 0200113 A	05-11-86	JP 61264240 A	22-11-86
US 5104791 A	14-04-92	NONE	